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=> file reg; d rn cn 12; d rn cn 13
FILE 'REGISTRY' ENTERED AT 15:45:43 ON 21 FEB 2003
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STRUCTURE FILE UPDATES:    20 FEB 2003  HIGHEST RN 492991-99-3
DICTIONARY FILE UPDATES:   20 FEB 2003  HIGHEST RN 492991-99-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L12  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   123515-51-5  REGISTRY
CN   Bactericidal/permeability-increasing protein (human precursor) (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   1-193-Protein BPI (bactericidal/permeability-increasing) [132-alanine]
     human
CN   15: PN: US62[illegible]7 SEQID: 15 unclaimed protein
CN   16: PN: US60[illegible]01 SEQID: 13 unclaimed protein
CN   1: PN: W0010[illegible] SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W00018[illegible] SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W0[illegible] SEQID: [illegible] claimed protein
CN   [illegible]: PN: W000[illegible] SEQID: [illegible] claimed protein
CN   [illegible]: PN: W00071149 SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W00100658 SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W0104346 SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W0[illegible]44 SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: US6087126 SEQID: [illegible] claimed protein
CN   [illegible]: PN: W00104347 SEQID: [illegible] unclaimed protein
CN   [illegible]: PN: W00104348 SEQID: [illegible] claimed protein
CN   4: PN: US61[illegible]75 SEQID: 4 unclaimed protein
CN   14: PN: W00100671 SEQID: 15 unclaimed protein
CN   15: PN: W000[illegible]172 SEQID: 16 unclaimed protein
CN   Bactericidal/permeability-increasing protein (human)
CN   Bactericidal/permeability-increasing protein (human clone pING4322
     precursor)
CN   Bactericidal/permeability-increasing protein (human clone seqid1
     precursor)
CN   DNA (human bactericidal and permeability-increasing protein cDNA plus
     flanks)
CN   DNA (human protein BPI (bactericidal/permeability-increasing) cDNA plus
     flanks)
CN   Glycoprotein BPI (human precursor protein moiety reduced)
CN   Glycoprotein BPI (human synthetic precursor)
CN   Protein (human bactericidal/permeability-increasing BPI precursor)
```

CN Protein (human bactericidal/permeability-increasing precursor)
CN Protein BPI (bactericidal/permeability-increasing (human clone seqid1 precursor)
CN Protein BPI (bactericidal permeability-increasing) (human clone pING1742 precursor)
CN Protein BPI (human bactericidal permeability-increasing precursor)
CN Protein BPI (human bactericidal permeability-increasing precursor deletion derivative)
CN Protein BPI (human bactericidal permeability-increasing)
CN Protein BPI (human clone pING1742 bactericidal/permeability-increasing)
CN Protein BPI (435-valine) (human bactericidal permeability-increasing precursor)

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **162493-47-2** REGISTRY
CN DNA (human bactericidal/permeability-increasing protein (DNA plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (human bactericidal/permeability-increasing protein messenger RNA-complementary plus 5'- and 3'-flanking regions fragment)
OTHER NAMES:
CN 3: PN: US6765197 SEQID: 3 unclaimed DNA

=> file caplus; d que l1c; d que l14
FILE 'CAPLUS' ENTERED AT 10:40:34 ON 21 FEB 2003
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FILE COVERS 1907 - 21 Feb 2003 VOL 138 ISS 9
FILE LAST UPDATED: 20 Feb 2003 (20030220/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L1	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON L3515-41-3 RN
L2	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON 162493-47-2 RN
L4	52	SEA	FILE=CAPLUS	ABB=ON	PLU=ON L2 OR L3
L5	40569	SEA	FILE=CAPLUS	ABB=ON	PLU=ON BPI OR (BACTERICID? OR PERMEAB? 3A) PROTEIN
L6	14276	SEA	FILE=CAPLUS	ABB=ON	PLU=ON MENING?
L7	72	SEA	FILE=CAPLUS	ABB=ON	PLU=ON L4 OR L5 AND L6
L8	39	SEA	FILE=CAPLUS	ABB=ON	PLU=ON L7 AND PY=1996
L9	6	SEA	FILE=CAPLUS	ABB=ON	PLU=ON L7 AND AY=1996
L10	9	SEA	FILE=CAPLUS	ABB=ON	PLU=ON L7 AND PY<=1996

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L11            43 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR L9 OR L10
L12             9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND PHARMACT/SC,SX



L2              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  1[illegible]-51[illegible]-[illegible]/RN
L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  16[illegible]-[illegible]/RN
L4             5[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 OR L3
L5           4039 SEA FILE=CAPLUS ABB=ON  PLU=ON  BPI OR (BACTERICID? OR
                  PERMEAB?) (3A) PROTEIN
L6          1427[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  MENIN[illegible]
L7             7[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  (L4 OR L5) AND L6
L8             3[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND PY<=1996
L9              [illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND AY<=1996
L10             [illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 AND PRY<=1996
L11            4[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR L9 OR L10
L12             [illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND PHARMACT/SC,SX
L13            3[illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 NOT L12
L14             [illegible] SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND (RBPI OR TOPOLOGY)/TI


=> s l12 or l14
L39          13 L12 OR L14

=> file medline; d que l1[illegible]
FILE 'MEDLINE' ENTERED AT 16:4[illegible] ON [illegible] FEB [illegible]03

 FILE LAST UPDATED: 21 FEB 200[illegible] ([illegible]21/UP).  FILE COVERS 19[illegible] TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ[illegible].html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L15           42[illegible] SEA FILE=MEDLINE ABB=ON  PLU=ON  BACTERICIDAL PERMABILITY
                  INCREASING PROTEIN/CN OR BPI
L16          618[illegible] SEA FILE=MEDLINE ABB=ON  PLU=ON  MENINGOCOCCAL INFECTIONS+NT/CT

L17          4698 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEISSERIA MENINGITIDIS+NT/CT
L18             [illegible] SEA FILE=MEDLINE ABB=ON  PLU=ON  L15 AND (L16 OR L17)
L19             0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L18 AND PY<=199[illegible]


=> file embase; d que l26
FILE 'EMBASE' ENTERED AT 16:41:02 ON [illegible] FEB 2003
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 FILE COVERS 1974 TO 20 Feb 2003 (20030220/ED)

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 substance identification.
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L20           197 SEA FILE=EMBASE ABB=ON  PLU=ON  BACTERICIDAL PERMEABILITY
                  INCREASING PROTEIN/CT
L21           413 SEA FILE=EMBASE ABB=ON  PLU=ON  BPI
L22          1610 SEA FILE=EMBASE ABB=ON  PLU=ON  MENINGOCOCCOSIS/CT
L23           740 SEA FILE=EMBASE ABB=ON  PLU=ON  EPIDEMIC MENINGITIS/CT
L24          5407 SEA FILE=EMBASE ABB=ON  PLU=ON  NEISSERIA MENINGITIDIS/CT
L25             [illegible] SEA FILE=EMBASE ABB=ON  PLU=ON  (L20 OR L21) AND (L22 OR L23
                  OR L24)
L26             0 SEA FILE=EMBASE ABB=ON  PLU=ON  L25 AND PY<=1996


=> file biosis; d que l31
FILE 'BIOSIS' ENTERED AT 14:41:04 ON 21 FEB 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 19 February 2003 (20030219/ED)

L27           567 SEA FILE=BIOSIS ABB=ON  PLU=ON  BPI
L28          4161 SEA FILE=BIOSIS ABB=ON  PLU=ON  MENING?
L29            10 SEA FILE=BIOSIS ABB=ON  PLU=ON  L27 AND L28
L31             2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L29 AND PY<=1996


=> file wpids; d que l34
FILE 'WPIDS' ENTERED AT 14:41:17 ON 21 FEB 2003
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FILE LAST UPDATED:            18 FEB 2003       <20030218/UP>
MOST RECENT DERWENT UPDATE:       200312         <200312/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L32           213 SEA FILE=WPIDS ABB=ON  PLU=ON  (BACTERICID? OR PERMEAB?) (3W)
                  PROTEIN
L33           184 SEA FILE=WPIDS ABB=ON  PLU=ON  BPI? OR RBPI?
L34          2155 SEA FILE=WPIDS ABB=ON  PLU=ON  MENING?
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L35           6 SEA FILE=WPIDS ABB=ON  PLU=ON  (L32 OR L33) AND L34
L36           5 SEA FILE=WPIDS ABB=ON  PLU=ON  L35 NOT (FHM OR HAEMOP? OR
                ANEMIA)/TI
L38           3 SEA FILE=WPIDS ABB=ON  PLU=ON  L36 AND PRY<=1996



=  dup rem l39 l38 l31
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PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L38
PROCESSING COMPLETED FOR L31
L40          15 DUP REM L39 L38 L31 (3 DUPLICATES REMOVED)
                ANSWERS '1-13' FROM FILE CAPLUS
                ANSWERS '14-15' FROM FILE BIOSIS

= d ibib ab l40 1-15

L40 ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2003 ACS        DUPLICATE 1
ACCESSION NUMBER:          1998:647[illegible]  CAPLUS
DOCUMENT NUMBER:           129:26[illegible]
TITLE:                     Therapeutic uses of N-terminal BPI protein
                           products in ANCA-positive patients
INVENTOR(S):               Carroll, Stephen Fitzhugh
PATENT ASSIGNEE(S):        USA
SOURCE:                    U.S. Pat. Appl. Publ., 11 pp., Cont. of U.S. Ser. No.
                           742,965, abandoned.
                           CODEN: USXXCO
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

      PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
      ----------------    ----  --------      ----------------  --------
      US 20021179916      A1    2002[illegible]  US 1999-455245    19991222 <--
      US 6441796          B2    2002[illegible]
PRIORITY APPLN. INFO.:                    US 1996-742965    B1 19961101 <--
AB    Improved therapeutic uses for N-terminal bactericidal/
      permeability-increasing (BPI) protein products
      are described in patients that have BPI-reactive anti-neutrophil
      cytoplasmic antibodies.  Antibodies reactive against BPI among
      ANCA-pos. subjects suggests that these antibodies may interfere with the
      beneficial activities of BPI.  BPI-reactive
      autoantibodies bind to BPI holoprotein but have very little
      reactivity with N-terminal BPI products.  The N-terminal
      BPI protein products can be used in patients suffering from
      hemorrhagic trauma, infection, and inflammatory diseases.

L40 ANSWER 2 OF 15  CAPLUS  COPYRIGHT 2003 ACS        DUPLICATE 2
ACCESSION NUMBER:          1998:3[illegible]  CAPLUS
DOCUMENT NUMBER:           12[illegible]:19652
```

TITLE: Therapeutic uses of **BPI** protein products in cystic fibrosis patients
INVENTOR(S): Carroll, Stephen Fitzhugh; Scannon, Patrick J.; Gavit, Patrick D.
PATENT ASSIGNEE(S): Xoma Corporation, USA; Carroll, Stephen Fitzhugh; Scannon, Patrick J.; Gavit, Patrick D.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9[illegible]	A1	1[illegible]	WO 199[illegible]	1[illegible] <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9[illegible]	A1	1[illegible]	AU 199[illegible]	1[illegible] <--
AU [illegible]	B2	[illegible]		
EP [illegible]	A1	[illegible]	EP 199[illegible]	1[illegible] <--
EP [illegible]	B1	[illegible]		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP [illegible]	T2	[illegible]	JP 199[illegible]	1[illegible] <--
AT [illegible]	E	[illegible]	AT 199[illegible]	1[illegible] <--

PRIORITY APPLN. INFO.: US 1996-74298[illegible] A 1[illegible] <--
WO 1997-US[illegible] W 1[illegible]

AB Improved therapeutic uses and formulations for **BPI** (**bactericidal permeability**-increasing **protein** products are described in cystic fibrosis patients.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 1997:[illegible] CAPLUS
DOCUMENT NUMBER: 128:[illegible]
TITLE: Therapeutic uses of **bactericidal permeability**-increasing **BPI protein** products for human **meningococcemia**
INVENTOR(S): Giroir, Brett P.; Scannon, Patrick J.
PATENT ASSIGNEE(S): Xoma Corporation, USA; Giroir, Brett P.; Scannon, Patrick J.
SOURCE: PCT Int. App., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742966	A1	19[illegible]	WO 199[illegible]	1[illegible] <--
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DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, MZ, SD, SL, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

AU 9[illegible]	A1	19[illegible]	AU 1997-3[illegible]	1[illegible] <---
AU [illegible]	B2	20[illegible]		
EP 914144	A1	19[illegible]	EP 1997-[illegible]	1[illegible] <---
EP 914144	B1	20[illegible]		
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US [illegible]	B1	20[illegible]	US 1999-[illegible]	1[illegible] <---
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			US 1997-[illegible] A1	1[illegible]
			US 1998-[illegible] A1	1[illegible]
			US 1999-[illegible] A1	1[illegible]

AB Methods and materials for the treatment of human **meningococcemia** are provided in which therapeutically effective amts. of **BPI** protein products are administered.

L40 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:[illegible] CAPLUS
DOCUMENT NUMBER: 135:[illegible]
TITLE: 18P-**BPI** fusion recombinant endotoxin-neutralizing proteins with longer half-life and without triggering undesirable immune response
INVENTOR(S): Scott, Randal W.; Marra, Marian N.
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: U.S., [illegible] pp., Cont.-in-part of Appl. No. PCT/US97/[illegible].
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US [illegible]	B1	20[illegible]	US 1998-[illegible]	1[illegible] <---
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EP [illegible]	A1	1999[illegible]	EP 1997-[illegible]	1[illegible] <---
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WO [illegible]	A1	1997[illegible]	WO 1997-US[illegible]	1[illegible] <---
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
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WO [illegible]	A1	1998[illegible]	WO 1997-US[illegible]	1[illegible] <---
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO [illegible]	A1	1998[illegible]	WO 1997-US[illegible]	1[illegible] <---
W: AU, CA, JP				

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     RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
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    US [illegible]146761    A1    2002[illegible]        US [illegible]-[illegible]14[illegible]     [illegible]518 <--
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                                              US [illegible]       A[illegible] [illegible] <--
                                              WO [illegible]       A[illegible] [illegible] <--
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                                              WO [illegible]       W  [illegible]0501 <--
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AB In general, the invention features a recombinant endotoxin-neutralizing polypeptide (RENP) characterized by (i) an amino acid sequence, (ii) an amino acid sequence and structure that facilitates selective and specific binding to lipopolysaccharide and which once bound to the lipopolysaccharide, provides endotoxin-neutralizing activity. Preferably, the RENP is composed of an amino acid sequence similar to, but not identical to, an amino acid sequence of two mol. endotoxin-binding proteins, lipopolysaccharide binding **protein** (LBP) and **bactericidal permeability**-increasing (**BPI**), or both. Preferably, the RENP contains an LPS-binding domain derived from the amino acid sequence of **BPI**, LBP, or both. Preferably, the RENPs are covalently bound to a mol. which enhances the half-life of the polypeptide. For example, the half-life enhancing mol. can be an Ig fragment, a half-life detn. portion of LBP or LBP deriv., or polyethylene glycol. The RENPs of the invention can be used in pharmaceutical compns. for therapeutic and prophylactic regimens, as well as in various in vitro and in vivo diagnostic methods. An advantage of the present invention is that the endotoxin-neutralizing proteins have a half-life in serum which is enhanced relative to the half-life of naturally-occurring LPS-binding proteins, and bind LPS without triggering a significant, undesirable immune response. **BPI** and L1-[illegible]B2[illegible]-4[illegible] were successfully expressed in the methylotrophic yeast Pichia pastoris. The results of the investigation of **BPI** efficacy in rats with either (a) hemorrhagic shock or (b) endotoxic shock show that (a) in rats with hemorrhagic shock, the mortality was decreased from [illegible]/10 ([illegible]) control group to 2/10 ([illegible]) **BPI** group at 4[illegible] h; (b) in rats with endotoxic shock, the [illegible]-day mortality was significantly reduced (p=0.[illegible]) by **BPI** treatment to 43%, as compared to [illegible]% in the control group. Plasma LPS levels were at least partially neutralized at two hours ([illegible].+-.4.1 vs [illegible].+-.4.[illegible] ng/mL). Cytokine formation was concomitantly reduced in the **BPI** group as measured by plasma TNF levels at two hours ([illegible].+-.[illegible] vs 11.[illegible].+-.[illegible] ng/mL). Liver transaminases (GOT and GPT, whose elevation indicates hepatic dysfunction) and bilirubin still increased at eight hours; however, the increase was less with **BPI**. These data demonstrate that **BPI** has utility as a therapeutic agent against endotoxin-related disorders in hemorrhagic as well as endotoxic shock. FIG. 19 shows that endotoxin-neutralizing proteins such as **BPI** and L1-[illegible](1[illegible]3->[illegible]) B2[illegible]-456(N206-[illegible]) ([illegible]) can also neutralize endotoxin-mediated TNF release in the lung. These results indicate that these proteins are effective when delivered directly into the lung and thus may be useful for treatment of pneumonias and other endotoxin-related disorders of the lung, such as ARDS.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:26257 CAPLUS
DOCUMENT NUMBER: 126:42713
TITLE: Recombinant endotoxin-neutralizing proteins
INVENTOR(S): Scott, Randal W.; Marra, Marian N.
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621456	A1	19960718	WO 1996-US1095	19960116 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6174857	B1	20010116	US 1995-431517	19950501 <--
AU 9646319	A1	19960731	AU 1996-46319	19960116 <--
PRIORITY APPLN. INFO.:			US 1995-431517 A	19950501 <--
			US 1989-341034 B2	19890421 <--
			US 1990-466680 A2	19900116 <--
			US 1990-547016 B2	19900629 <--
			US 1991-661511 A2	19910228 <--
			WO 1991-US2578 A2	19910418 <--
			US 1992-915720 A2	19920716 <--
			US 1993-56182 B2	19930430 <--
			US 1993-149711 B2	19931110 <--
			WO 1994-US4704 A2	19940429 <--
			WO 1996-US1095 W	19960116 <--

AB In general, the invention features a recombinant endotoxin-neutralizing polypeptide (RENP) characterized by (i) an amino acid sequence, (ii) an amino acid sequence and structure that facilitates selective and specific binding to lipopolysaccharide and (iii) once bound to the lipopolysaccharide, provides endotoxin-neutralizing activity. Preferably, the RENP contains an LPS-binding domain derived from the amino acid sequence of **BPI**, LBP or both. Preferably, the RENP contains an LPS-binding domain derived from the amino acid sequence of **BPI**, LBP or both. Preferably, the RENPs are covalently bound to a mol. which enhances the half-life of the polypeptide. The RENPs of the invention can be used in pharmaceutical compns. for therapeutic and prophylactic regimens, as well as in various in vitro and in vivo diagnostic methods.

L40 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:549594 CAPLUS
DOCUMENT NUMBER: 121:149749
TITLE: Improved therapeutic compositions comprising **bactericidal/permeability**-increasing (**BPI protein** products
INVENTOR(S): Lambert, Lewis H., Jr.
PATENT ASSIGNEE(S): Xoma Corporation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421436	A1	19940929	WO 1994-US2695	19940316 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2103[illegible] AA 1[illegible] CA 1993-2103[illegible] 1[illegible]
AU 9[illegible] A1 1[illegible] AU 1993-[illegible] 1[illegible]
AU 7[illegible] B2 2[illegible]
EP 8[illegible] A1 1[illegible] EP 1993-[illegible] 1[illegible]
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
JP 1[illegible] T2 1[illegible] JP 1993-[illegible] 1[illegible]
EP 1[illegible] A2 2[illegible] EP 1[illegible] 1[illegible]
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
PRIORITY APPLN. INFO.: US 1992-[illegible] A 1[illegible]
US 1993-[illegible] A 1[illegible]
EP 1993-[illegible] A3 1[illegible]
WO 1993-[illegible] W 1[illegible]

AB Improved therapeutic compns. having enhanced antimicrobial activity comprising a **bactericidal permeability**-increasing (**BPI**) **protein** product and a **bactericidal** -activity enhancing polyoxyethylene block copolymer surfactant (poloxamer surfactant) or a bacterial and fungal growth-inhibiting enhancing polyoxamer surfactant, with EDTA, and methods for treating bacterial infection by administering such compns., alone or concurrently with antibiotics.

L49 ANSWER [illegible] OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1[illegible] CAPLUS
DOCUMENT NUMBER: 1[illegible]
TITLE: Characterization of the structural elements in lipid A required for binding of a recombinant fragment of **bactericidal/permeability**-increasing **protein rBPI23**. [Erratum to document cited in CA[illegible]]
AUTHOR(S): Gazzano-Santoro, Helene; Parent, James B.; Conlon, Paul J.; Kussler, Herbert G.; Tsai, Chao-Ming; Lill-Elghanian, Deborah A.; Hollingsworth, Pawle I.
CORPORATE SOURCE: Sepsis Res. Dep., XOMA Corp., Berkeley, CA, 94710, USA
SOURCE: Infection and Immunity (**1995**), 63(12), 4967
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstr. or the index entries.

L49 ANSWER [illegible] OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1[illegible] CAPLUS
DOCUMENT NUMBER: 1[illegible]
TITLE: Characterization of the structural elements in lipid A required for binding of a recombinant fragment of **bactericidal permeability**-increasing **protein rBPI23**
AUTHOR(S): Gazzano-Santoro, Helene; Parent, James B.; Conlon, Paul J.; Kussler, Herbert G.; Tsai, Chao-Ming; Lill-Elghanian, Deborah A.; Hollingsworth, Pawle I.
CORPORATE SOURCE: Sepsis Research Department, XOMA Corporation, Berkeley, CA, 94710, USA
SOURCE: Infection and Immunity (**1995**), 63(6), 2211-5
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both human **bactericidal/permeability**-increasing **protein** (**BPI**) and a recombinant N-terminal fragment of **BPI** (rBPI23) have been shown to bind with high affinity to the lipid A region of lipopolysaccharide (LPS). In the present study, lipid A preps. derived from bacterial LPS as well as synthetic lipid A's and various lipid A analogs were used to det. the structural elements required for rBPI23 binding. rBPI23 bound in vitro to a variety of synthetic and natural lipid A preps. (both mono- and diphosphoryl forms), including lipid A's prepd. from Escherichia coli and Salmonella, Neisseria, and Rhizobium species. Binding does not require that the origin of neg. charge be phosphate, since rBPI23 bound with high affinity to lipid A's isolated from Rhizobium species that contain carboxylate (Rhizobium trifolii) or sulfate (Rhizobium meliloti) anionic groups and lack phosphate. Lipid A acyl chains are important, since rBPI23 did not bind to four synthetic variants of the .beta.(1-6)-linked D-glucosamine disaccharide lipid A prod group, all devoid of acyl chains. rBPI23 also bound weakly to lipid X, a monosaccharide lipid precursor of LPS corresponding to the reducing half of lipid A. Lipid IVA, a precursor identical to E. coli lipid A except that it lacks the 2' and 3' acyl chains, was the simplest structure identified in this study that rBPI23 bound with high affinity. These results demonstrate that rBPI23 has a binding specificity for the lipid A region of LPS and binding involves both electrostatic and hydrophobic components.

L40 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995: 43159 CAPLUS
DOCUMENT NUMBER: 122:7745
TITLE: Effect of a recombinant N-terminal fragment of **bactericidal/permeability**-increasing **protein** (**rBPI23**) on cerebrospinal fluid inflammation induced by endotoxin
AUTHOR(S): Kartalija, Marinka; Kim, Young; White, Mark L.; Nau, Roland; Turner, Jay H.; Taeuber, Martin G.
CORPORATE SOURCE: Infectious Diseases Laboratory, San Francisco General Hospital, San Francisco, CA, 94143, USA
SOURCE: Journal of Infectious Diseases (**1995**), 171(1), 148-53
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endotoxin triggers the subarachnoid inflammation of gram-neg. **meningitis**. This study examd. the ability of a recombinant N-terminal fragment of **bactericidal/permeability** -increasing **protein** (rBPI23) to block endotoxin-induced **meningitis** in rabbits. Intracisternal (i.c.) injection of 15-20 ng of **meningococcal** endotoxin induced high cerebrospinal fluid (CSF) concns. of tumor necrosis factor (TNF) and CSF pleocytosis and increased CSF lactate concns. Co-administration of rBPI23 significantly reduced **meningococcal** endotoxin-induced TNF release into CSF ($P < .005$), lactate concns. ($P < .001$), and CSF white blood cell counts ($P < .01$). No such effect was found in animals receiving i.v. rBPI23. Concns. of rBPI23 in CSF were high after ic administration but low or undetectable after systemic administration. Thus, high concns. of rBPI23 can effectively neutralize **meningococcal** endotoxin in CSF, but low CSF concns. after systemic administration currently limit its potential usefulness as adjunctive drug treatment in gram-neg. **meningitis**.

L40 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:555668 CAPLUS
DOCUMENT NUMBER: 121:155668
TITLE: Recombinant human **bactericidal**/**permeability**-increasing **protein** (**rBPI23**) is a universal lipopolysaccharide-binding ligand
AUTHOR(S): Appelmelk, B. J.; An, Yan-Qing; Thijs, Bart G.; MacLaren, David M.; Graaff, Johannes
CORPORATE SOURCE: Dep. Med. Microbiology, Vrije Univ., Amsterdam, 1081 BT, Neth.
SOURCE: Infection and Immunity (**1994**), 62(8), 3564-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A recombinant 23-kDa protein (rBPI23) derived from human **bactericidal**/**permeability**-increasing **protein** (**BPI**) possesses potent endotoxin-neutralizing abilities in vitro and in vivo. Binding of rBPI23 to those endotoxins (lipopolysaccharides [LPSs]) encountered clin. would be a prerequisite for efficacy in decreasing mortality among patients suffering from gram-neg. sepsis and shock, a disease state in which an endotoxin role for LPS has been implicated. rBPI23 binds well to lipid A, to rough-mutant O-chain-deficient LPS (Re to Ra chemotypes), to lipid A-core covalently linked to the O chain, to LPSs from clin. relevant serotypes, and to bacterial cells of Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae, the species most often implicated in clin. gram-neg. sepsis and shock. Significant binding of rBPI23 to these antigens took place at rBPI23 concns. of 1-100 ng/mL (median, 16-32 ng/mL). Binding did not involve 3-deoxy-D-manno-octulosonate of the inner core. Detg. the exact epitope recognized by rBPI23 would require further studies with synthetic lipid A substructures. The demonstrated ability of rBPI23 to universally bind LPS provides a sound basis for further testing of its endotoxin-neutralizing abilities, including clin. trials.

L41 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:479711 CAPLUS
DOCUMENT NUMBER: 119:79711
TITLE: The 5C protein of Neisseria **meningitidis** is highly immunogenic in humans and induces bactericidal antibodies
AUTHOR(S): Rosenqvist, Einar; Hoiby, E. Arne; Wedege, Elisabeth; Klingenberg, Karina; Achtman, Mark
CORPORATE SOURCE: Dep. Vaccine Bacteriol., Natl. Inst. Public Health, Oslo, Norway
SOURCE: Journal of Infectious Diseases (**1993**), 167(5), 1065-73
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5C protein is expressed by the strain of N. **meningitidis** (44/76) used for prodn. of the Norwegian **meningococcal** group B outer membrane vesicle vaccine and is included in the final formulation of this vaccine. The IgG antibody response to 5C in vaccinees, in systemic **meningococcal** disease, and carriers was measured using ELISAs with synthetic liposomes as antigen and by immunoblotting. Increased levels of IgG were found in paired sera from all 3 groups. The antibodies were bactericidal to **meningococci** of serogroups A and B that expressed large amts. of 5C but not to **meningococci** expressing smaller amts. There was a linear correlation between bactericidal titer and units of IgG to 5C.

L43 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:579[illegible] CAPLUS
DOCUMENT NUMBER: 117:1[illegible]
TITLE: Cloning of Neisseria **meningitidis** protein P64k gene and vaccines containing the protein
INVENTOR(S): Silva Rodriguez, Ricardo; Selman Houssein Sosa, Manuel; Guillen Nieto, Gerardo; Herrera Martinez, Luis Saturnino; Fernandez Mas, Julio Raul; Novoa Perez, Lidia Ines; Morales Grillo, Juan; Rivera Cordova, Vivian; Gonzalez Blanco, Sonia; et al.
PATENT ASSIGNEE(S): Centro de Ingenieria Genetica y Biotecnologia, Cuba
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English.
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP [illegible]	A2	[illegible]	EP 1991-[illegible]	[illegible]
EP [illegible]	A3	[illegible]		
EP [illegible]	B1	[illegible]		
FI [illegible]	A	[illegible]	FI 1991-[illegible]	[illegible]
IN [illegible]	A	[illegible]	IN 1991-[illegible]	[illegible]
CA [illegible]	AA	[illegible]	CA 1991-[illegible]	[illegible]
AU [illegible]	A1	[illegible]	AU 1991-[illegible]	[illegible]
AU [illegible]	B2	[illegible]		
US [illegible]	A	[illegible]	US 1991-[illegible]	[illegible]
AT [illegible]	E	[illegible]	AT 1991-[illegible]	[illegible]
ES [illegible]	T3	[illegible]	ES 1991-[illegible]	[illegible]
BR [illegible]	A1	[illegible]	BR 1991-[illegible]	[illegible]
JP [illegible]	A2	[illegible]	JP 1991-[illegible]	[illegible]
JP [illegible]	B4	[illegible]		

PRIORITY APPLN. INFO.: CU 1991-115 A 19900917
AB The N. **meningitidis** P64k protein gene is cloned. The gene was cloned and expressed in Escherichia coli. It was produced to the extent of [illegible]% of the total cellular protein. Monoclonal antibodies to this **protein** had significant **bactericidal** titers against other N. **meningitidis** serogroups, serotypes, and subtypes. Other vaccines were prepd., i.e., a protein contg. the variable epitopes of the N. **meningitidis** P1.15 protein fused to P64k, an Haemophilus influenzae polysaccharide-P64k conjugate, and a bivalent vaccine contg. hepatitis B surface antigen and P64k. Segments of P64k had significant sequence similarity to E. coli acetyltransferase and lipoamide acetyltransferase.

L43 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:[illegible] CAPLUS
DOCUMENT NUMBER: 117:[illegible]
TITLE: The class 1 outer membrane protein of Neisseria **meningitidis**: prediction of **topology** and construction of a multivalent vaccine strain
AUTHOR(S): Van der Ley, P.; Poolman, J. T.
CORPORATE SOURCE: Natl. Inst. Public Health Environ. Prot., Bilthoven, Neth.
SOURCE: Neisseriae 1990, Proc. Int. Pathog. Neisseria Conf., 7th, **1991**, Meeting Date 1990, 235-40.
Editor(s): Achtman, Mark. de Gruyter: Berlin, Germany.
CODEN: 59FUAF

DOCUMENT TYPE: Conference
LANGUAGE: English
AB In order to asses the role of class 1 **protein** in inducing **bactericidal** antibodies, mice were immunized with outer membrane vesicles (OMV) prepns. from a set of isogenic derivs. of strain H44/76. Mutational removal of class 3 protein had no effect on the bactericidal titer, whereas removal of class 1 protein resulted in a strong strong redn.. None of the strains induced bactericidal antibodies against the heterologous strain 2996; however, the addn. of only the class 1 gene from that strain to H44/76 resulted in a bactericidal titer almost as high as that obtained with 2996 itself. These results clearly demonstrate the dominant role of class 1 protein in the induction of bactericidal antibodies with OMV prepns., and also indicate that a multivalent vaccine based on different subtypes of this protein should be feasible.

L40 ANSWER 14 OF 15 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: PREV1996[illegible]
TITLE: Issues in the adjunct therapy of severe sepsis.
AUTHOR(S): Verhoef, Jan (1); Hustinx, Willem M. N.; Frasa, Helma; Hoepelman, Andy I. M.
CORPORATE SOURCE: (1) Eijkman-Winkler Inst. Med. and Clinical Microbiol., Division Infectious Diseases, Univ. Hosp., Heidelberglaan 100, 3584 CX Utrecht Netherlands
SOURCE: Journal of Antimicrobial Chemotherapy, (1996) Vol. 38, No. 2, pp. 167-182.
ISSN: 0305-7453.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Until recently the concept of immunomodulation in patients with severe sepsis (formerly called sepsis syndrome or septic shock) appeared very promising. Research has focused on the possible therapeutic potential of interfering with cytokine pathways, either by preventing the induction of cytokines, such as TNF-alpha, by neutralization of lipopolysaccharide (LPS), or through the use of agents that attenuate cytokine action. Nowadays research on protein or protein constructs with antibacterial activities such as bacterial permeability increasing protein (**BPI**), platelet activating factor receptor antagonists, nitric oxide and cyclooxygenase inhibitors, are still being followed. In large clinical trials monoclonal antibodies against core glycolipid (E5, HA1A) were shown to be at best of only marginal benefit, and in some trials results were inconclusive. Also, the results with IL-1ra, although initially heralded with high expectation, were at the end disappointing and the trials discontinued. Two large trials with monoclonal antibodies against TNF showed some effect in subcategories of patients; a third trial is on its way. Other phase I, II studies include those of soluble TNF receptors and **BPI**. The area of immunomodulation has now become an area of more realism and the results of early trials has forced investigators to go back to the drawing board and to re-investigate the whole concept of immunotherapy and immunoprophylaxis.

L40 ANSWER 15 OF 15 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: PREV1999[illegible]
TITLE: Protection of bovine brain endothelial cell (BBEC) injury from endotoxins: Role of bactericidal/permeability increasing protein (**BPI**) and anti-lipid A monoclonal antibody (MAb.
AUTHOR(S): Arditi, Moshe; Zhou, Jin; Kim, Kwang Sik
CORPORATE SOURCE: Childrens Hosp. Los Angeles, Univ. Southern Calif. Sch. Med., Los Angles, CA USA

SOURCE: Pediatric Research, (1993) Vol. 33, No. 4 PART 2, pp. 161A. Meeting Info.: 103rd Annual Meeting of the American Pediatric Society and 62nd Annual Meeting of the Society for Pediatric Research Washington, D.C., USA May 3-6, 1993 ISSN: 0031-3998.
DOCUMENT TYPE: Conference
LANGUAGE: English

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